UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte WADE D. WALKE, NATHANIEL L. WILGANOWSKI, and
C. ALEXANDER TURNER, JR.

Appeal 2007-3881
Application 09/833,782
Technology Center 1600

Decided: September 24, 2007

Before TONI R. SCHEINER, ERIC B. GRIMES, and NANCY J. LINCK, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to polynucleotides. The Examiner has rejected the claims as lacking patentable utility. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

BACKGROUND

The Specification discloses "human polynucleotides encoding a protein sharing sequence similarity with mammalian neurolysin proteins" (Spec. 1: 9-11). "Neurolysins are soluble proteins of the zinc

metalloprotease family that bind and cleave protein substrates such as angiotensin and neurotensin (typically between pro and tyr residues). As such, neurolysins have been implicated in a number of biological processes and anomalies such as blood pressure regulation, kidney function, pain management, cardiac disease, natriuresis and diabetes." (*Id.* at 1: 24-30).

DISCUSSION

1. CLAIMS

Claims 1-5 are pending and on appeal. Claim 3 is representative and reads as follows:

3. An isolated nucleic acid molecule comprising a nucleotide sequence encoding the amino acid sequence shown in SEQ ID NO: 2.

Claim 3 is directed to a polynucleotide encoding the protein described in the Specification as a "human protein . . . shar[ing] structural similarity with animal neurolysins and angiotensin-binding proteins" (Spec. 2: 5-10).

2. UTILITY

Claims 1-5 stand rejected under 35 U.S.C. §§ 101 and 112, first paragraph, as lacking patentable utility. The Examiner acknowledges that the Specification "discloses that the claimed polynucleotide encodes a protein[ ] which shares structural similarities with mammalian neurolysin" (Answer 9). The Examiner also acknowledges that "[a]t the time [the] application was filed the function of neurolysin was well established for mammals. . . . The characteristic features of neurolysin [are] that it cleaves neurotensin between residues Pro10 and Tyr11, and that it binds angiotensin." (*Id.* at 10.) The Examiner specifically states, in fact, that "the

utility of animal neurolysins was already known before the instant application was filed" (*id.* at 18).

However, the Examiner concluded that the established utility of animal neurolysins cannot be imputed to the protein of SEQ ID NO: 2 because Appellants "*do not assert the function of the encoded protein as being that of neurolysin*. Nowhere in the specification is there any statement that suggests that the disclosed protein shares *functional similarity* to mammalian neurolysins." (*Id.* at 9.) The Examiner cites several references in support of her position that "the state of the art clearly teaches the unpredictability of assigning function based on sequence homology and acknowledges that small changes in amino acid sequence can drastically change function" (*id.* at 10).

Appellants argue that the "biological significance and function of neurolysin and neurolysin like metalloproteases are well known to those of skill in the art" (Br. 6, citing Kato et al., J. Biol. Chem. 272: 15313-15322 (1997)).[1] Appellants assert that "a sequence that is *identical at the amino acid level* over the entire length of the described sequence" has been deposited in GenBank and annotated (by others) as human neurolysin (Br. 4-5). Appellants conclude that "[t]herefore, it is clear that the amino acid sequence of SEQ ID NO: 2 encodes [sic] human neurolysin" (*id.* at 5).

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[1] Appellants also cite two other references in support of the quoted statement, but the other references were published after the effective filing date of the instant application and therefore cannot be relied on to show the state of the art at the time the invention was made. "Enablement, or utility, is determined as of the application filing date." *In re Brana*, 51 F.3d 1560, 1567 n.19 (Fed. Cir. 1995).

The Examiner disputes the significance of the Kato reference and GenBank entry, asserting that the researchers who deposited the GenBank sequence

> have, thus far, not disclosed actual enzymatic activity of the protein set forth by SEQ ID NO: 2 . . . which they call neurolysin. Search indicates that [the deposit] has not been followed by any publication . . . showing that this sequence does in fact have neurolysin activity. Thus, all [t]hat is currently known of "human neurolysin" is a DNA and amino acid sequence which shows structural homology to pig, rat, mouse and rabbit enzyme.

(Answer 15-16.) The Examiner asserts that "nowhere in [Kato] one can find the word 'neurolysin'" (*id.* at 18).

We will reverse the rejection. The Examiner bears the initial burden of showing that a claimed invention lacks patentable utility. *See In re Brana*, 51 F.3d 1560, 1566 (Fed. Cir. 1995) ("Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility."). "Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans." *Id.*

Here, the Examiner has acknowledged that "the utility of animal neurolysins was already known before the instant application was filed" (Answer 18). Therefore, the relevant issues are (1) whether those of skill in the art would have understood the Specification to disclose that SEQ ID NO: 2 has the same activity as neurolysin, and (2) whether the evidence of

record adequately shows that SEQ ID NO: 2 is likely to share neurolysin's activity.

The Specification states that SEQ ID NO: 2 "shar[es] sequence similarity with mammalian neurolysin proteins" (Spec. 1: 10-11); that neurolysins are metalloproteases that "cleave protein substrates such as angiotensin and neurotensin" (*id.* at 1: 24-26) and have been implicated in a number of diseases; and that "neurolysins can act as therapeutics as well as drug targets (*id.* at 1: 29-30). The Specification does not disclose that SEQ ID NO: 2 is similar to any protein other than neurolysin or disclose any other function or activity that it is likely to have. In view of the Specification's focus on neurolysin and the disclosure that SEQ ID NO: 2 shares structural similarity with known neurolysins, we agree with Appellants that those skilled in the art would have understood the Specification to disclose that SEQ ID NO: 2 is a neurolysin and likely to share the activity of other, known neurolysins.

We also agree with Appellants that the evidence of record does not support the Examiner's position that the structural similarity between SEQ ID NO: 2 and other neurolysins is unlikely to translate into functional similarity.

Appellants rely on a GenBank entry as evidence that SEQ ID NO: 2 is human neurolysin (Br. 4-5). The GenBank entry is post-filing evidence and therefore can be relied on only to support an assertion in the Specification, not to add substantively to the Specification's disclosure. *See In re Hogan*, 559 F.2d 595, 605 n.17 (CCPA 1977). In this case, the GenBank entry can be relied on to support the implicit assertion in the Specification that SEQ ID

NO: 2 is a neurolysin. The Examiner does not dispute that the GenBank entry's amino acid sequence is identical to SEQ ID NO: 2 or that the researchers who deposited the GenBank entry annotated it as human neurolysin. We therefore agree with Appellants that the GenBank entry is persuasive evidence that SEQ ID NO: 2 is the human neurolysin sequence.

The Examiner has conceded that "the utility of animal neurolysins was already known before the instant application was filed" (Answer 18). Kato provides evidence supporting the Examiner's statement.[2] Kato provides a thorough discussion of research on neurolysin (also known as endopeptidase 24.16, oligopeptidase M, and MOP) (Kato, paragraph bridging 15313 and 15314). Kato states that neurolysin and endopeptidase 24.15 are "the two best characterized" mammalian metalloendopeptidases (*id.* at 15313, right-hand column) and that neurolysin inactivates neurotensin and has been shown to "have a relatively broad substrate-specificity and tissue distribution" (*id.* at 15314, left-hand column).

It is true, as the Examiner points out, that Appellants have pointed to no experimental data, in the instant Specification or elsewhere, that shows definitively that the protein of SEQ ID NO: 2 has the activity of neurolysin. However, a patent applicant need not provide definitive experimental data in order to show that a claimed invention has patentable utility. Rather, the Examiner bears the burden of showing a reasonable basis for doubting the

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[2] The Examiner states that "nowhere in [Kato] one can find the word 'neurolysin,'" but Kato states that "[t]he enzyme, termed neurolysin or endopeptidase 24.16, was shown to be distinct from EP 24.15 (TOP) . . ." (Kato at 15314, middle of left-hand column).

utility of a claimed invention. *See In re Langer*, 503 F.2d 1380, 1391 (CCPA 1974).

After the Examiner has challenged the asserted utility of a claimed invention and the Applicant has provided evidence or argument in rebuttal, the merits of the rejection must be re-evaluated in light of all the evidence of record, and patentability determined based on a preponderance of the evidence. *See In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992): "After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the record, by a preponderance of the evidence with due consideration to persuasiveness of argument."

In this case, the Examiner's rejections are not supported by a preponderance of the evidence of record. The rejections under 35 U.S.C. §§ 101 and 112, first paragraph, for lack of utility are reversed.

REVERSED

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